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EXAMINER	
GRASER, JENNIFER E	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 04/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,281	MANGOLD ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-19,44 and 50-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-19, 44 and 50-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.11

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/15/05 has been entered.

Claims 16-19, 44 and 50-64 are currently pending.

Claim Rejections - 35 USC § 112

2. Claims 16-19, 44 and 50-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claims 16, 19 and 59, the amino acid sequence of EA1, e.g., SEQ ID NO:1 or the deposited antibody, should be inserted in the claims. The mere recitation of a name, i.e., EA1, to describe the invention is not sufficient to satisfy the Statute's requirement of adequately describing and setting forth the inventive concept. The claim should provide any structural properties, such as the amino acid sequence of the protein or molecular weight, which would allow for one to identify the protein without ambiguity. The mere recitation of a name does not adequately define the claimed antibody. The antigen to which the antibody binds is a critical limitation. While the specification can be used to provide definitive support, the claims are not read in a

vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

Claims 16, 19, 53, 54 and 59 are vague and indefinite because the claims recite that the isolated antibody or fragment thereof bind the EA1 antigen of B.anthracis, yet they also state that the antibody binds spores or vegetative cells of B.anthracis. The latter part of the claim makes it unclear that the antibody is binding to the EA1 antigen. This wording is confusion. Is the antibody binding to the EA1 antigen on the spores or vegetative cells of B.anthracis? If so, clarification should be made. If not, it is unclear what the antibody is binding to.

Claims 17-19 are vague and confusing due to the phrase "which incorporates". It is unclear what is meant by 'the kit incorporates'. Does the kit contain or comprise these elements? The use of the term 'incorporates' is vague and indefinite in this context. Amendment is required.

Claim 54 contains two periods. One of the periods must be deleted.

Claim 62 is vague and indefinite due to the phrase "and wherein said antibody is *optionally* a monoclonal antibody". The phrase "optionally" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. In general, when an ingredient in a claim is 'optional' it is not viewed as being part of the invention. Clarification and correction is required.

Claim 64 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: there is no correlation step, e.g., what does detecting the complex tell one? Additionally, what type of sample is used?

Claim Rejections - 35 USC § 112-Deposit Requirement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 58 and 63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of hybridoma ATCC deposit accession No. PTA-2632. Because it is not clear that the properties of this antibody are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the best mode disclosed by the specification requires the use of the hybridoma, a suitable deposit for patent purposes is required. Accordingly, filing of evidence of the reproducible production plasmids, one of ordinary skill in the art could be assured to the ability to practice the invention as claimed. Exact replication of the hybridoma is an unpredictable event.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of the deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and full street address of the depository is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

© the deposits will be maintained in a public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become non-viable or non-replicable.

In addition, a deposit of the biological material that is capable of self-replication either directly or indirectly must be viable at the time of the deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1)The name and address of the depository;

2)The name and address of the depositor;

3)The date of deposit;

4)The identity of the deposit and the accession number given by the depository;

5)The date of the viability test;

6)The procedures used to obtain a sample if the test is not done by the depository; and

7)A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 16, 44, 50-54, and 56-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Mesnage et al (Molec. Microbiol. 1997, 2346): 1 147-1 155).

Mesnage et al teach isolated antibodies to the Bacillus anthracis S-layer component, **EAI**. The major cell antigen to which the isolated antibodies bind in the Mesnage reference is 100% identical to the EAI protein disclosed by Applicants and set forth in SEQ ID NO: 1. It is taught that a Western blot assay suggested that the antibodies were highly specific to B.anthracis and did not cross-react. See page 1150-

1151. Electron microscopy using grids with rabbit anti-EAI antibodies or rabbit anti-sap antibodies, or on anti-sap antibodies. The grids were incubated on colloidal gold anti-rabbit or anti-mouse coupled antibodies. The Western blots and grids performed with the EA1 antibodies anticipate the method of claim 64 as they include contacting an antibody/fragment with a sample, forming a complex and detecting said complex.

Applicants have disclosed in the instant specification that antibodies directed against this EAI protein are antibodies which bind to B.anthracis, but do not bind to B.thuringiensis. These antibodies are disclosed as the preferred embodiment in the instant specification. Although the reference does not specifically recite that the antibody to B.anthracis does not specifically react with B.thuringiensis, it inherently would not since the antigen to which it binds is specific to B.anthracis and the instant specification supports this finding. The antibodies to the EAI protein would be identical to Applicant's antibodies to the EAI antibody, i.e., the antibodies are raised against the same antigen. There are no structural differences between the prior art antibody, e.g., specifically binds EA1 antigen of B.anthracis, and those that are instantly claimed. The intended use of the claimed composition does not patentably distinguish the composition, *per se*, since such undisclosed use is inherent in the reference composition; e.g., does not bind *B.thuringiensis* or *B.cereus*. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed

invention and the prior art in order to patentably distinguish the claimed invention from the prior art. An antibody produced from the hybridoma deposited as PTA-2632 would also possess the same binding capabilities of the claimed fragments and antibodies.

Since the Patent Office does not have the facilities for examining and comparing Applicant's antibody with the antibody of the prior art, the burden of proof is upon applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 195 USPQ 430, 433 (CCPA 19&&). Since the instant kit claims do not require any components other than the antibodies, the reference anticipates the claims. The phrase "diagnostic kit" is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Response to Applicants' Arguments:

Applicants argue that Mesnage teach the production of rabbit polyclonal antibodies in sera against EA1 polypeptide and that there is no indication that this antiserum was specific for B.anthracis. This has been fully and carefully considered but is not deemed persuasive. The scope of the instant claims includes polyclonal antibodies, particularly polyclonal antibodies generated from any source. Polyclonal antibodies specifically raised against a defined antigen, e.g., EA1, would 'specifically bind' that antigen. It is irrelevant that Mesnage do not provide cross-reaction studies

against B.thuringenienis or B.cereus, the antibodies are structurally the same to that which is claimed and, therefore, would inherently possess the same binding capabilities. Applicants argue that the intended use of their antibodies 'does not bind B.thuringiensis or B.cereus' is enough to distinguish over the prior art of record. This is not deemed persuasive. There are no structural differences between the prior art antibody, e.g., specifically binds EA1 antigen of B.anthracis, and those that are instantly claimed. The intended use of the claimed composition does not patentably distinguish the composition, *per se*, since such undisclosed use is inherent in the reference composition; e.g., does not bind *B.thuringiensis* or *B.cereus*. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting. There is nothing in the clams which distinguishes the structure of the antibody with the antibodies taught by Mesnage. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. An antibody produced from the hybridoma deposited as PTA-2632 would also possess the same binding capabilities of the claimed fragments and antibodies.

Additionally, Mesnage specifically teach that a Western blot assay suggested that the antibodies (to EA1) were highly specific to B.anthracis and did not cross-react. See page 1150-1151.

Since the Patent Office does not have the facilities for examining and comparing Applicant's antibody with the antibody of the prior art, the burden of proof is upon applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 195 USPQ 430, 433 (CCPA 19&&).

Applicants arguments about Mesnage not modifying his antibodies to be specific for B.anthracis are moot since the antibodies taught by Mesnage are structurally identical to the antibodies recited in the instant claims. Accordingly, they would possess identical properties.

It is especially noted that the instant claims allow for fragments of antibodies as well and do not require the antibody to bind to any specific epitope along the EA1 polypeptide. The language of the instant claims allow for the antibody to bind to any epitope or epitopes of the EA1 antigen. The antibody taught by Mesnage binds to an antigen which is 100% identical to the antigen to which Applicants' antibody binds. Accordingly, since the antibodies claimed are structurally the same, e.g, bind EA1 antigen, they would inherently possess the same cross-reactive properties.

Since the Patent Office does not have the facilities for examining and comparing Applicant's antibody with the antibody of the prior art, the burden of proof is upon applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 195 USPQ 430, 433 (CCPA 19&&).

Claim Rejections - 35 USC § 103

7. Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mesnage et al (Molec. Microbiol. 1997, 23(6): 1147-1 155), as applied to claims 16, 44, 50-54, and 56-63 above, in view of Loomis et al (WO 99/64863).

Mesnage et al teach antibodies to the Bacillus anthracis S-layer component, EAI. It is disclosed that EAI constitutes the main lattice of the B.anthracis S-layer, and is the major cell-associated antigen. See abstract. Antibodies to the surface array protein (Sap) are also taught. It is taught that a Western blot assay suggested that the antibodies were highly specific to B.anthracis and did not cross-react. See page 1150-1151. Electron microscopy using grids with rabbit anti-EAI antibodies or rabbit anti-sap antibodies, or on anti-sap antibodies. The grids were incubated on colloidal gold anti-rabbit or anti-mouse coupled antibodies. The major cell antigen to which the isolated antibodies bind in the Mesnage reference is 100% identical to the EAI protein disclosed by Applicants. Applicants have disclosed in the instant specification that antibodies directed against this EAI protein are antibodies which bind to B.anthracis, but do not bind to B.thuringiensis. These antibodies are disclosed as the preferred embodiment in the instant specification. However, Mesnage et al does not particularly exemplify the use of these antibodies in a colloidal particle based lateral flow detection system.

Loomis et al teach that colloidal gold particle immunoassays have been successfully used in the prior art for many years. See pages 1-3. Loomis et al teach a more sensitive immunoassay test to what was known in the art. It is a colloidal colorimetric flow through and lateral flow assay. The entire test is conducted on a test strep and the detection antibody is preferably a FAB fragment that has been labeled

with a 5O-100mm gold particle and immobilized on a test pad. See page 4. It is taught that the use of capture dendrimers to align and secure capture antibodies on a solid surface insure that no immunological activity of the capture antibody is sterically hindered.

It would have been prima facie obvious to one of ordinary skill in the art to use the antibodies taught by Mesnage et al in a colloidal lateral flow detection system as taught by Loomis et al to detect B.anthracis because Mesnage et al teach that the antibodies are highly specific to B.anthracis and that EAI constitutes the main lattice of the B.anthracis S-layer, and is the major cell-associated antigen. One of ordinary skill in the art would have a reasonable expectation that a specific antibody developed against the major cell-associated antigen of a bacterium to be very effective in detecting the bacterium in a sample. Loomis et al teaches that it is a highly sensitive detection assay which is simple, sensitive and specific. The use of the EAI and/or Sap antibodies taught by Mesnage in a colloidal lateral flow detection system would have been obvious as a B.anthracis detection system. The assembly of the reagents to these assays in a diagnostic kit would have been obvious to one of ordinary skill in the art at the time the invention was made for convenience and storage capabilities.

Response to Applicants' Arguments:

Applicants arguments are directed to the Mesnage reference. These arguments were addressed in the 'Response to Applicants' Arguments' section under the 102 Mesnage rejection above.

9. Claim 55 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mesnage et al (Molec. Microbiol. 1997, 23(6): 1147-1 155), as applied to claims 16, 44, 50-54, and 56-63 above, in view of Kohler et al (Science. 1986. 233: 1281-1285)

The teachings of Mesnage are set forth above. However, they do not specifically teach monoclonal antibodies to the EA1 antigen.

Kohler et al teach that making monoclonal antibodies to known antigens was common and have greater specificity than polyclonal antibodies and can be readily produced in great quantities.

It would have been obvious to one of ordinary skill in the art at the time the invention was made that monoclonal antibodies to the EA1 antigen could be generated/used in place of polyclonal antisera because it was well known in the prior art as evidenced by Kohler that, in general, monoclonal antibodies have proven superior to polyclonal antisera both in terms of production and clinical utility. Polyclonal antisera are not only costly and labor intensive to produce, but they are also difficult to quality control because each immunized rabbit can produce only so much antisera and every new rabbit is different. Therapeutically, monoclonals can more precisely impact a target, often with fewer adverse effects and greater specificity. Accordingly, one of ordinary skill in the art would have been motivated to make monoclonal antibodies to the EA1 antigen.

Status of Claims:

No claims are allowed. Applicants have been arguing a distinct and unexpected antibodies, yet that antibody is not claimed. The antibodies instantly claimed do not

structurally differ from those taught in the prior art. If Applicants can demonstrate that an antibody generated from their hybridoma is structurally different from that known in the prior art, then the antibody made from the hybridoma should be claimed- along with specific evidences filed to demonstrate it is unique from that of the prior art.

11. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is (703) 872-9306 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Friday from 7:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

Jennifer Graser
Primary Examiner
Art Unit 1645

4/5/02